VIP AND PACAP REGULATE GLIAL SECRETION OF CYTOKINES AND GROWTH FACTORS: IMPLICATIONS FOR NEURODEVELOPMENT AND THE TREATMENT OF NEURODEGENERATIVE DISEASE.

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Vasoactive intestinal peptide (VIP) has been shown to be a neurotrophic peptide in CNS cultures and a growth-promoting regulator in early postimplantation mouse embryos. Both actions appear to involve indirect mechanisms. In vitro studies have indicated that the survival-promoting activity associated with VIP is mediated indirectly through the secretagogue action of VIP on astroglia. Eight cytokines (IL-1 alpha and beta, IL-3, IL-6, TNF-alpha, interferon gamma, G-CSF and M-CSF), many with recognized neurotrophic activity, have been recovered in the medium of cultured astroglia stimulated with 0.1nM VIP. IL-1 alpha, in particular, has been shown to promote neuronal survival under conditions of electrical blockade. VIP-related peptides [peptide T, pituitary adenylate cyclase activating peptide (PACAP)] that also exhibit neurotrophism produce the release of these cytokines, albeit with reduced potency and efficacy. In addition, VIP releases activity dependent neurotrophic factor (ADNF) from glia. An active peptide of ADNF is shown to prevent cell death associated with NMDA, beta amyloid peptide and the HIV envelope protein. These data indicate that multiple neurotrophic substances are released from glia by VIP, some of which may provide a means for the treatment of neurodegenerative disease.